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Total Number of Pages in This Submission	13

Application Number	09/974,712
Filing Date	10/10/01
First Named Inventor	Friddle
Group Art Unit	1647
Examiner Name	R. S. Landsman
Attorney Docket Number	LEX-0251-USA

ENCLOSURES *(check all that apply)*

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  - [ ] Affidavits/declaration(s)
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SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Lexicon Genetics Incorporated Lance K. Ishimoto Reg. No. 41,866
Signature	Lance K. Ishimoto by Peter G. Sefarian Reg No 40162
Date	July 29, 2004

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as Express mail label EV322477886US addressed to: Commissioner for Patents, MS Appeal Brief - Patents, P.O. Box 1450, Alexandria, VA 22313 on: July 29, 2004

Typed or printed name	Nancy Stacey		
Signature	Nancy Stacey	Date	July 29, 2004

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant(s): Friddle *et al.*	Group Art Unit: 1647
Application No.: 09/974,712	Examiner: R. Landsman
Filed: October 10, 2001	Attorney Docket No.: LEX-0251-USA
Title: Polynucleotides and Polypeptides Encoding Human Ion Channel Proteins (As Amended)	

REPLY BRIEF

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TABLE OF CONTENTS

TABLE OF AUTHORITIES

CASES

STATUTES

REPLY BRIEF

Sir:

Appellants hereby submit an original and two copies of this Reply Brief to the Board of Patent Appeals and Interferences ("the Board") in response to the Examiner's Answer mailed on June 3, 2004. March 5, 2004. This Reply Brief is thus due August 3, 2004 and is timely submitted.

Appellants believe no additional fees are due in connection with this Reply Brief. However, should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason related to this communication, the Commissioner is authorized to charge any underpayment or credit any overpayment to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

I. REAL PARTY IN INTEREST

Appellants agree with the Examiner's assertion that "A statement identifying the real party in interest is contained in the brief" (Examiner's Answer at page 1).

II. RELATED APPEALS AND INTERFERENCES

Appellants agree with the Examiner's assertion that "A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief" (Examiner's Answer at page 1- 2).

III. STATUS OF THE CLAIMS

Appellants agree with the Examiner's assertion that "The statement of the status of the claims contained in the brief is correct" (Examiner's Answer at page 2).

IV. STATUS OF THE AMENDMENTS

Appellants agree with the Examiner's assertion that "The appellant's statement of the status of

amendments after final rejection contained in the brief is correct" (Examiner's Answer at page 2).

V. SUMMARY OF THE INVENTION

Appellants agree with the Examiner's assertion that "The summary of invention contained in the brief is essentially correct" (Examiner's Answer at page 2).

VI. ISSUES ON APPEAL

Appellants agree with the Examiner's assertion that "The appellant's statement of the issues in the brief is correct." (Examiner's Answer at page 2).

VII. GROUPING OF THE CLAIMS

Appellants essentially agree with the Examiner's assertion that "The rejection of claims 1-3 and 5 stand or fall together because appellants brief does not include a statement that this grouping of claims does not fall together and reasons in support thereof" (Examiner's Answer at page 2). However Appellants note that they affirmatively stated that "For the purposes of the outstanding rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, the claims will stand or fall together." (Appeal Brief at page 3).

VIII. CLAIMS APPEALED

Appellants agree with the Examiner's assertion that "The copy of the appealed claims contained in the Appendix to the brief is correct" (Examiner's Answer at page 2).

IX. PRIOR ART OF RECORD

Appellants essentially agree with the Examiner's assertion as to the art previously presented by the Examiner in this case (Examiner's Answer at page 2-3).

X. ARGUMENT

A. Do Claims 1-3 and 5 Lack a Patentable Utility?

Appellants do not wish to restate all of the arguments presented in the Appeal Brief concerning the Examiner's allegation that claims 1-3 and 5 lack a patentable utility, and instead incorporate the entirety of Section VIII(A) of the Appeal Brief at this point herein by reference. However, Appellants feel the need to specifically address those areas of the Brief that contained arguments that were particularly unique to the present case and deemed non-persuasive by the Examiner in the Examiner's Answer (the "Answer") in some detail for the record.

First Appellants would like to note that in first paragraph of the Response to Argument section (Answer at page 6) the Examiner appears to favor an unusual standard. Appellants assertions are deemed "speculative"(line 4) based, it appears, on the Examiner's misplaced belief that data in the form of examples are required to support assertions in U.S. patent applications. Appellants note that it has long been established that "there is no statutory requirement for the disclosure of a specific example". *In re Gay*, 135 USPQ 311 (C.C.P.A. 1962). Appellants assertion of the stated utility is legally sufficient and should control the utility analysis unless the Examiner meets the burden of establishing the lack of utility by making evidence of record that conclusively refutes the Applicants asserted utility.

Appellants respectfully submit that the legal test for utility has involved an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Furthermore, this position is well established and was even recognized and reiterated under the newly installed utility guidelines, Applicants note that MPEP 2107 (II)(B)(1) states:

> (1) If the applicant has asserted that the claimed invention is useful for any particular practical purpose (i.e., it has a "specific and substantial utility") and the assertion would be

considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility. (MPEP 2107 (II)(B)(1))

The presently claimed sequences were asserted by Appellants in the specification to encode a novel human ion channel protein (specification in original title, on page 1, line12 and on lines 24-28), particularly potassium channels and more particularly a voltage-gated potassium channel protein (specification on page 2, lines 2-4). Further, the specification asserted (at or about page 13, lines 22-24) that the molecules of the present invention were expressed in, *inter alia*, the heart (at or about page 3, lines 31-34) and asserted that mutations in the presently claimed sequences could lead to alterations in cardiac related disorders such as arrhythmia and high blood pressure (page 13, lines 22-24).

Thus, in the specification as filed Appellants had asserted that the presently claimed voltage-gated potassium channel protein is expressed in the heart and plays a role in arrhythmia (heart disease). However, the Examiner deemed these assertions to be without merit, yet the Examiner failed to meet the burden of establishing the lack of utility by making evidence of record that conclusively refutes the Appellants' asserted utility. In contrast, Appellants then submitted several additional forms of evidence that indicated that their assertions were not only credible, but correct. Appellants submitted evidence that indicated that the presently claimed sequences had been recognized by others of skill in the art, third party scientists, *in no way affiliated with Appellants*, as encoding a human voltage-gated potassium channel protein, which these scientists gave the name *Homo sapiens* voltage-gated potassium channel KCNA7. The sequences of the protein identified as voltage-gated potassium channel KCNA7 is 99.781 % identical at the amino acid level and, not surprisingly after the first 38 bases, 99.927 % identical to the presently claimed nucleic acid sequences. Clearly the evidence of record supports Appellant's assertions that the sequences of the present invention encode a novel human ion channel, in particular a voltage-gated potassium channel (a variant of KCNA7). In addition, Appellants also submitted third party confirmation that Appellants' assertions regarding the role of the novel human protein encoded by the presently claimed sequences and mutations in the same, in human disease, including heart disease. The specification stated "mutant NHP allele (*e.g.*, a person manifesting a NHP-associated phenotype" (specification at page 13,

line 12)). As described in the scientific publication previously submitted, "Characterization of the human voltage-gated potassium channel gene, KCNA7, a candidate gene for inherited cardiac disorders, and its exclusion as a cause of progressive familial heart block I (PFHBI)"(Bardien-Kruger, S., *et al.*, Eur J Hum Genet, 10(1):36-43, 2002), those of kill in the art clearly recognized that the a mutation in the gene encoding the claimed sequences could be involved in human inherited cardiac disorders, for this was the basis of the study on which this publication reports. Clearly those of skill in the art would have recognized Appellants' assertions as to the involvement of the claimed sequences in human cardiac disorders, such as arrhythmia, as absolutely credible.

One of the key issues raised in this Appeal is the validity of Example 10 of the PTO's Revised Interim Utility Guidelines Training Materials (pages 53-55), which establishes that a rejection under 35 U.S.C. § 101 as allegedly lacking a patentable utility and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility, is not proper when there is no reason to doubt the asserted utility of a full length sequence (such as the presently claimed sequence) that has a similarity score of 95% to a protein having a known function.

In the present case, clearly evidence supports Appellants' assertions that the sequences of the present invention encode a human voltage-gated potassium channel protein (KCNA7), a protein for which there is a well established utility (it is an ion channel that is expressed in the heart) that is recognized by those of skill in the art and whose asserted involvement in human heart disease was clearly credible to those of skill in the art at the time the application was filed. In addition, in the Analysis portion of Example 10 it states that "Based on applicant's disclosure and the results of the PTO search, there is no reason to doubt the assertion...that if there is a well-established utility already associated with the claimed invention, the utility need not be asserted in the specification as filed...Thus the conclusion reached from this analysis is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not be made" (emphasis added).

Throughout prosecution of this case, the Examiner has failed to submit any objective evidence that Appellants' assertions were not credible and has chosen to refer to these assertions as "speculative" based solely on his subjective opinion, while at the same time essentially ignoring the evidence. In contrast,

Appellants have submitted several forms of third party evidence that indeed indicate that those of skill in the art would have readily viewed their functional assertions as credible (for when faced with the same facts made the same assertions) and, thus, under the newly installed utility guidelines the Examiner has improperly imposed a rejection based on a lack of utility.

> (1) If the applicant has asserted that the claimed invention is useful for any particular practical purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility. (MPEP 2107 (II)(B)(1))

Despite the Examiner's allegations to the contrary, it is clear that the present case is similar to that presented in Example 10 of the Revised Interim Utility Guidelines Training Materials (pages 53-55). In the present case it is clear that the sequences of the present invention encode a human ion channel protein, a voltage gated ion channel (KCNA7). The Examiner dismisses Appellants' continued assertions that the protein of the present invention is a voltage gated ion channel (KCNA7) and that the function of voltage gated ion channels as a class of proteins and KCNA7 specifically are well known to those of skill in the the art. However, according to the guidelines the conclusion reached from this analysis is that a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph, utility rejection should not have been made. Thus, the rejection of the presently claimed invention under a 35 U.S.C. § 101 and a 35 U.S.C. § 112 first paragraph utility rejection should be overruled.

Additionally the Examiner's Answer also attempts to revive and reiterates the Examiner's previously stated position that sequence homology and the relationship between structure and function is not generally accepted by those of skill in the art. In support of this position the Examiners Answer attempts to revive and describe once again several contrarian articles that have been previously presented and rebutted by the Appellant. The Examiner did not, however, maintain this position and address Appellants rebuttals and as such appeared to have conceded the point. Procedural issues aside, the fact remains that none of these articles constitute direct evidence that Appellants' assertion that the sequences

of the present invention encode a human voltage gated ion channel (KCNA7) as none of the cited articles describe the protein of the present invention, nor even proteins of the same class.

To summarize, Appellants position on this handful of unrelated and contrarian publications, this "relevant literature" does not in fact support the concept that function cannot be based on sequence and structural similarity, in contrast many of the examples actually support the use of such methodologies while identifying several areas in which caution should be exercised. As stated previously these inaccuracies and potential pitfalls can be overcome by a more careful analysis by those of skill in the art. Automatic methods of sequence homology identification was only the staring point for consideration the sequences of the present invention underwent careful analysis by a series of individuals of skill in the art, many highly qualified (multiple B.S. and Ph.D. level scientists).

As stated previously, while there may not be a 100% consensus within the scientific community regarding prediction of protein function from homology information, this is neither unusual nor is it indicative of a general lack of consensus. A few rare, and therefore publishable, exceptions do not a rule make.

One form of evidence supporting the position that bioinformatic information is recognized to be of value by those of skill in the art are the results of a recent search of the NCBI-NLM-NIH public scientific database "PubMed" using the term "bioinformatics" which resulted in 5,548 different scientific publications. If bioinformatic information is not useful in predicting protein function from structural homology information, why are so many publications reporting the results of its use?

A second form of evidence supporting the position that bioinformatic information is recognized to be of value by those of skill in the art is the fact that many scientists, corporations and institutions elect to allocate significant proportions of their limited resources for access to private bioinformatic systems and databases. Thus, it would appear obvious that those of skill in the art value and accept the results of bioinformatic analysis for they are willing to allocate a significant portion of their limited resources for access to such information. Presumptively, if those of skill in the art believed this information to be invalid, they would not do so.

A third, and perhaps the most persuasive, form of evidence supporting the position that bioinformatic information is recognized to be of value by those of skill in the art is the issuance of multiple

US patents regarding bioinformatic prediction and methods for doing the same (see for example, U.S. Patent Nos. 6,229,911, 6,567,540, 6,615,141, 6,631,331, 6,651,008, 6,677,114). Of particular interest might be U.S. Patent No. 6,466,874, one of whose claims reads "A method of identifying proteins as functionally linked, the method comprising comparing sequences to find homologous functional domains." Why would a U.S. Patent have issued on a method of carrying out an analysis that is without utility, an analysis that is not accepted by those of skill in the art as a credible method of predicting protein function from structural homology information? Issued patents are presumed to be valid and therefore, logically, one must presume that such an analysis has utility recognized by the USPTO.

In summary, the scientific evidence presented clearly supports the assertions made in the specification. The presently claimed sequences encode a human voltage-gated potassium channel protein (now also known as KCNA7). The function of voltage-gated potassium channel proteins, particularly those expressed in the heart, is well established and recognized by those of skill in the art. Furthermore, the presently claimed sequences encode a human voltage-gated potassium channel protein that as asserted in the specification as filed clearly was recognized by those of skill in the art at the time the application was filed to be involved in human heart disease. Thus, according to both the historic legal test for utility that involves assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable, and under the newly installed utility guidelines (MPEP 2107 (II)(B)(1), the presently claimed sequences which encode a human voltage-gated potassium channel protein (KCNA7) have specific and substantial, real world utility. Therefore for the above reasons, as well as the reasons set forth in Appellants' previous Responses and Appeal Brief, Appellants submit that the rejection of claims 1-3 and 5 under 35 U.S.C. § 101 should not have been made and should be overruled.

B. Are Claims 1-3 and 5 Unusable Due to a Lack of Patentable Utility?

Regarding the rejection of claims 1-3 and 5 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by either a clear asserted utility or a well-established utility, Appellants submit that as claims 1-3 and 5 have been shown to have "a specific, substantial, and credible utility", as detailed in Section X(A) above, as well as Section VIII(A) of the Appeal Brief, the present rejection of claims 1-3 and 5 under 35 U.S.C. § 112,

first paragraph, cannot stand.

Appellants therefore submit that the rejection of claims 1-3 and 5 under 35 U.S.C. § 112, first paragraph, must be overruled.

XI. CONCLUSION

Appellants respectfully submit that, in light of the foregoing arguments, the Final Action's conclusion that claims 1-3 and 5 lack a patentable utility and are unusable by the skilled artisan due to a lack of patentable utility is unwarranted. It is therefore requested that the Board overturn the Final Action's rejections.

Respectfully submitted,

July 29, 2004
Date

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